DEPARTMENT OF HEALTH AND HUMAN SERVICES

and

CENTERS FOR DISEASE CONTROL AND PREVENTION

convene the

ADVISORY COUNCIL FOR THE ELIMINATION OF TUBERCULOSIS

Atlanta, Georgia
October 6-7, 2004

RECORD OF THE PROCEEDINGS

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CENTERS FOR DISEASE CONTROL AND PREVENTION

ADVISORY COUNCIL FOR THE ELIMINATION OF TUBERCULOSIS
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Draft Minutes of the Meeting

The Department of Health and Human Services (HHS) and the Centers for Disease Control and Prevention (CDC) convened a meeting of the Advisory Council for the Elimination of Tuberculosis (ACET). The proceedings were held on October 6-7, 2004 at CDC's Corporate Square Facility, Building 8, in Atlanta, Georgia.

Opening Session

Dr. Masae Kawamura, the ACET Chair, called the meeting to order at 8:41 a.m. on October 6, 2004. She welcomed the attendees to the proceedings and opened the floor for introductions. The following individuals were present for the deliberations.

ACET Members
Dr. Masae Kawamura, Chair
Dr. Jeffrey Douglas
Dr. Michael Fleenor
Dr. Jennifer Flood
Dr. Richard Fluck
Ms. Teresa Garrett
Dr. David Gonzales
Ms. Sara Loaiza
Ms. Eileen Napolitano

***Ex Officio*s and Liaisons**
Dr. William Baine (AHRQ)
Ms. Duiona Baker (SAMHSA)
Dr. Henry Blumberg (IDSA)
Dr. Raymond Chinn (HICPAC)
Ms. Fran Du Melle (ATS)
Dr. Miguel Escobedo (U.S.-Mexico BHC)
Ms. Kim Field (NTCA)
Ms. Caroline Freeman (OSHA)
Dr. Fred Gordin (ATS)
Dr. Michael Kurilla (NIH/NIAID)
Dr. Michael Puisis (NCCHC)
Dr. Lee Reichman (ACCP)
Dr. Gary Roselle (VA)
Dr. Diana Schneider (DIHS)
Dr. Eva Solorzano (U.S.-Mexico BHC)
Ms. Rachel Stricof (APIC)
Dr. Litjen Tan (AMA)
Ms. Terry Tannenbaum (IUATLD)
Dr. Nancy Warren (APHL)
Dr. Theresa Watkins-Bryant (HRSA)
Dr. David Weissman (NIOSH)

Designated Federal Official
Dr. Ronald Valdiserri,
Executive Secretary

CDC Representatives
Dr. Janet Collins
(NCHSTP Acting Director)
Dr. Kenneth Castro, DTBE Director
Dr. Rachel Albalak
Dr. Jose Becerra
Dr. Terence Chorba
Ms. Ann Cronin
Ms. Hazel Dean
Mr. Nick Donaldson
Ms. Thena Durham
Ms. Mollie Ergle (Contractor)
Mr. Al Forbes
Ms. Paulette Ford-Knights
Ms. Judy Gibson
Dr. Reuben Granich
Dr. Dale Hu
Dr. Michael Iademarco
Dr. John Jereb
Ms. Lauren Lambert
Ms. Ann Lanner
Ms. Lilia Manangan
Mr. Chris McLaughlin
Ms. Suzanne Marks
Dr. Jerry Mazurek
Mr. Michael Melneck
Dr. Thomas Navin
Dr. Richard O'Brien
Dr. Adelisa Panlilio
Mr. Paul Poppe
Mr. Charles Schable
Dr. Thomas Shinnick
Ms. Brooke Steele
Dr. Zachary Taylor
Dr. Andrew Vernon
Dr. Wanda Walton

Guests
Ms. Asma Henry (Public)
Mr. Kevin Landkrohn (OSHA)
Dr. Charles Nolan (ATS)
Ms. Patricia Rivera (Emory University)
Dr. Sarah Royce (California DHS)
Mr. John Seggerson (NCET)

Dr. Ronald Valdiserri, the ACET Executive Secretary, informed the participants that ACET meetings are open to the public and all comments made during the proceedings are a matter of public record. He pointed out that an overview of the Federal Advisory Committee Act (FACA) was placed in the meeting packets to inform ACET of the federal law governing the business of FACAs. All FACA members are special government employees during their service and are required to submit financial disclosure forms on an annual basis to ensure no conflicts of interest exist. Members should be mindful of potential conflicts of interest identified by the CDC Office of Program Support and recuse themselves from voting or participating in these discussions.

Dr. Valdiserri described ACET's composition. Voting privileges are restricted to members only. Liaisons represent non-governmental organizations (NGOs) including professional organizations while *ex officios* represent federal agencies. Liaisons and *ex officios* have an interest and expertise in TB elimination and are invited to participate in all ACET discussions.

Update by the National Center for HIV, STD and TB Prevention (NCHSTP) Acting Director

Dr. Janet Collins covered the following areas in her report. One, Ms. Thena Durham, the NCHSTP Deputy Director for Policy, will be retiring at the end of 2004. The participants applauded her distinguished career at CDC and tremendous contributions to public health. Other personnel changes in NCHSTP include the outgoing Global AIDS Program (GAP) Director and an Acting Director for this position; a strong addition to the Office of the Associate Director for Science; and temporary details within other parts of CDC for the Associate Director for Planning and Policy and the Associate Director for Communications.

Two, the Division of AIDS, STD and TB Laboratory Research (DASTLR) was dissolved and its four branches were transferred to the NCHSTP Division of HIV/AIDS Prevention, Division of STD Prevention, and Division of Tuberculosis Elimination (DTBE) on October 1, 2004. International laboratory activities previously housed in DASTLR have now been transferred to GAP. A new laboratory support team has been established for this effort. The transition has been successful thus far; NCHSTP has already seen several advantages in fully integrating the laboratories in the respective content areas.

Three, CDC has not received its FY'05 budget and will operate under a continuing resolution with FY'04 funds through November 20, 2004. If the House bill is approved, FY'05 funding for TB control will be $2.4 million more than the FY'04 level. The House Appropriations Committee expressed concern about the number of new TB cases in foreign-born persons and urged CDC to collaborate with the U.S. Citizenship and Immigration Services to develop novel TB screening strategies for persons immigrating from countries with a high TB incidence. However, the House Appropriations Committee noted its satisfaction with DTBE's efforts and the reduction in TB cases.

If the Senate bill is approved, FY'05 funding for TB control will be $3.2 million more than the FY'04 level. The Senate Appropriations Committee pointed out that CDC's new TB funding formula is a "major step forward" and urged CDC to use the increased dollars to "maximize the percentage of TB control funds available on a per-case basis, while ensuring no state receives less funding than in FY'04." The entire structure of the Senate Appropriations budget for CDC is being reformatted and will result in several profound changes, such as separate line items for CDC's indirect costs and programmatic areas. Under this structure, for example, TB dollars will be directly allocated to DTBE and will not be further tapped by the Office of the CDC Director or NCHSTP. The House will adopt the new budget table in the future. CDC is pleased about the proposed TB increases and acknowledges the efforts of its external partners in educating and informing Congressional members about TB.

Four, CDC gave a detailed briefing to high-level HHS officials on the new TB budget formula in September 2004. HHS was extremely supportive of the new formula and questioned whether CDC could implement the plan on a faster time-line. Beginning in January 2005, 20% of core TB dollars will be awarded to states according to formula. CDC must comply with Congressional language in allocating new dollars, but hopes to use any new funds resulting from the FY'05 appropriation to offset the impact of the formula and ensure states do not experience reduced funding.

Five, the Advisory Committee to the CDC Director has received proposals from several internal offices requesting that expanded visions and directions be considered under the Futures Initiative. For example, the Office of Minority Health (OMH) asked to be housed in the new Office of Strategy and Innovation (OSI). Since OSI will be charged with establishing goals to guide CDC's focus areas and funding priorities, OMH's proposal ensures that CDC's goals will be consistent with and reflect health disparity issues. The proposal also calls for OMH to broaden its vision beyond racial/ethnic disparities, expand its core functions, and change its name to the "Office of Health Equity." The OMH Director presented the proposal in August 2004. NCHSTP committed to distributing the proposal to ACET before the meeting adjourned and also offered to forward ACET's comments about the document to the Advisory Committee to the CDC Director.

Ms. Durham was pleased that ACET and CDC will continue to strongly emphasize TB. She was confident that this focus will indeed accomplish the goal of eliminating TB. She was honored to participate with ACET and CDC in this effort over the years.

DTBE Director's Report

Dr. Kenneth Castro extended an apology on behalf of Dr. Mitchell Cohen, Director of the Coordinating Center for Infectious Diseases, for being unable to attend the meeting as scheduled. Dr. Cohen would attempt to attend the meeting at some point to answer ACET's questions about changes related to the Futures Initiative. Dr. Castro covered the following areas in his report. One, senior personnel changes in DTBE include the upcoming retirement of the Deputy Director, Mr. Paul Poppe, and the addition of a new Mycobacteriology Laboratory Branch Chief, Dr. Tom Shinnick.

Two, DTBE created a new budget formula to distribute TB dollars due to the changing TB epidemiology and anticipated level funding. Specific criteria were established by reviewing the five-year average of areas with the most significant morbidity and complexity in managing TB cases. Under the redistribution plan, TB dollars will be allocated to grantees with 40% of TB incident cases, 15% of U.S.-born minorities, 15% of foreign-born persons, 10% of Class A, BI and B2 TB, 5% of HIV/TB co-infection, 5%

of multidrug-resistant TB (MDR-TB), 5% of substance abusers, and 5% of homeless populations. Based on the formula, 21 FY'05 grantees will sustain reductions, 31 will receive increases, and 16 that receive ≤$200,000 will not be affected.

Correctional populations are not a specific category in the formula, but will be addressed due to overlap with some of the other groups. DTBE is maintaining a strong focus on this population through its ongoing involvement in updating CDC's 1996 guidelines for TB prevention and control in correctional facilities. DTBE extensively solicited input from external partners in developing the formula and launched a broad communication initiative both verbally and in writing. DTBE hosted web-based seminars, briefed TB controllers, distributed "Dear Colleague" letters, and made presentations to ACET and other groups.

Three, the House and Senate bills for additional TB control dollars are modest increases that do not reflect the cost of living. The federal funding gap is clearly documented and analyzed in a report by the National Coalition for the Elimination of Tuberculosis (NCET). The current TB budget resulted in decreased capacity for the Tuberculosis Epidemiologic Studies Consortium (TBESC) and Tuberculosis Trials Consortium (TBTC) to conduct programmatically relevant activities, but efforts are underway to leverage funds from other sources. TBTC and the Global Alliance for TB Drug Development (Alliance) will hold a meeting to explore potential collaborations with European companies that will allocate dollars for TB research. TBTC and Bayer will engage in discussions about TBTC's ongoing studies with moxifloxacin and its interest in evaluating moxifloxacin as a potential anti-TB drug. TBTC is also considering the National Institutes of Health (NIH) as a possible source of funding for clinical trials. The next TBTC meeting will be held in Atlanta on November 19-20, 2004.

Four, DTBE participated in recent outbreak investigations. A TB outbreak in Seattle, Washington involved recent immigrants of Eastern-African origin. The HIV infection rate was relatively high among the cases and substance abuse, prostitution and other risky behaviors were practiced. A TB cluster was detected in Mississippi, but the local health department did not have sufficient personnel to respond. DTBE has deployed a public health advisor to Fort Wayne, Indiana on a full-time basis for one year because the local infrastructure is insufficient to diagnose and treat active TB and latent TB infection (LTBI).

Five, DTBE and the CDC Procurement and Grants Offices are in negotiations to fund four regional training and medical consultation centers. Each site will be assigned a specific region of the country to provide medical consultation and implement TB training and education activities. DTBE will update ACET on this initiative at a future meeting after the awards have been announced. Six, all fifty states are now participating in universal genotyping and will send isolates to either the California or Michigan state

laboratory. This technology will play a significant role in strengthening knowledge of the dynamics of TB transmission and intervening earlier to interrupt transmission. Seven, a Futures Initiative concept is being pilot tested in which a CDC senior management officer will be assigned to oversee all cooperative agreements of a program.

Eight, the manufacturer of the QuantiFERON (QFT) Gold TB test has submitted a licensure application to the Food and Drug Administration (FDA). CDC convened an expert panel in May 2004 to review recommendations for the currently licensed QFT test and determine whether any of the existing guidelines should be revised if FDA approves the QFT-Gold application. FDA has requested CDC's assistance in reviewing appropriate labeling language. CDC expects to publish guidelines for QFT-Gold in the *Morbidity and Mortality Weekly Report* (*MMWR*) no later than three months following FDA approval. Nine, the infection control guidelines are in the final stages of CDC clearance and will soon be submitted to the *Federal Register* for a public comment period of 60 or 90 days.

Ten, DTBE is continuing to provide leadership and personnel to support the President's Emergency Plan for AIDS Relief (PEPFAR) and other global activities. DTBE is playing a key role in designing and implementing a technical strategy to determine whether routine HIV surveillance in TB clinics can be used to monitor the burden of disease, obtain accurate data on trends, and identify persons to place on anti-retroviral (ARV) drugs. This effort is being made in support of the World Health Organization (WHO) initiative to place 3 million persons on ARV drugs by the end of 2005. The Department of State has asked DTBE to detail a staff member to its office to assist in these activities. DTBE is attempting to identify factors contributing to high rates of TB and MDR-TB in several focus countries in Africa, Southeast Asia and Eastern Europe. Eleven, DTBE's efforts with NCET and other external partners to mobilize support for TB are ongoing. Twelve, DTBE is using the Program Assessment Rating Tool and Government Performance Results Act to monitor its progress in the TB elimination effort.

Advocacy for TB Elimination

Ms. Fran Du Melle is the ACET liaison representative for the American Thoracic Society (ATS). She outlined key sections of the Comprehensive Tuberculosis Elimination Act of 2003. The federal program would be renamed to the "National Program for Tuberculosis Elimination." ACET would advise the HHS Secretary on making progress toward TB elimination; create a national plan to consider recommendations by the Institute of Medicine (IOM); address the development and application of new technologies; and review progress toward TB elimination. For global initiatives, ACET would develop recommendations to guide U.S. involvement in global and cross-border

TB control activities with a focus on countries where a high incidence of TB directly affects the United States.

Priority would be given to TBESC and TBTC research and the development of regional capacity for TB prevention, control and elimination, particularly for low-incidence regions and populations disproportionately affected by TB. Public information and education programs would be expanded; support for Model Centers would continue; and collaborations with international organizations would be formalized through the Interagency Collaboration for the Elimination of Tuberculosis. ACET would provide annual reports on activities conducted under the National Program, including its opinion on the extent to which the IOM recommendations have been implemented. NIH would recreate the Tuberculosis Academic Award, develop a new Tuberculosis/Pulmonary Infection Award, and continue to emphasize recommendations published in the *U.S. Blueprint for TB Vaccine Development*.

The House and Senate bills for the legislation were introduced in May and August 2003, respectively, and then referred to the House Committee on Energy and Commerce and Senate Committee on Health, Education, Labor and Pensions. Cosponsors of the legislation include 67 in the House and 10 in the Senate, but minimal progress has been made because most cosponsors are in a different party than the current Administration. NCET's next step in this effort will be to host an integrated advocacy and communications planning session during the 109th Congress in November 2004.

The purpose of this important activity will be to identify policy, funding or legislative goals and priorities for new tools, international issues and domestic areas. This approach is being taken to ensure that the basic TB infrastructure is maintained at both domestic and global levels. The planning session will also be used as a forum to define roles and responsibilities for partner organizations in the areas of advocacy and communications. The primary goals for international TB efforts are to design strategies to allocate more funding to global partners through the U.S. Agency for International Development and develop new tools to improve TB control internationally. ACET was encouraged to attend the NCET training session on TB advocacy on February 23, 2005 in Vancouver, Canada.

Update on NCET Activities

Mr. John Seggerson of NCET conveyed that the organization is convened in collaboration with ATS, DTBE, the American Lung Association and National Tuberculosis Controllers Association (NTCA). NCET serves as a U.S. partner within the Stop TB Partnership and has a three-fold purpose. First, a channel of scientific and public health knowledge on the status of TB is made available to the public and

policymakers at global, national, state and local levels. Second, the public and policymakers are educated about the need to develop new tools and sustain community public health activities for TB elimination. Third, a framework is provided to increase community participation in the national TB effort with emphasis on building awareness and participation of at-risk populations.

NCET's composition includes two officers, two committees, two workgroups and members. The organizational membership includes government agencies, professional societies, NGOs, and national, state and local groups representing populations at high risk for TB. Individual members include TB controllers in states and large cities, health department staff, former TB patients, and persons who are from or support groups at high risk for TB. Both individual and organizational members have a strong interest in TB elimination. NCET does not have an exclusive membership and does not charge fees. Each NCET member is eligible to participate in activities.

The Steering Committee establishes NCET's overall policy and direction, while the Nominations Committee proposes potential officers. Government staff who serve on the Steering Committee as *ex officio* members have a limited role as technical advisors. The Coalition Building Workgroup has recommended that NCET focus on a few well-defined and key objectives each year. The workgroup is also charged with new membership. The Communications Workgroup is extensively involved with World TB Day each year and the Advocacy Workgroup recently completed a major survey with NTCA of external TB advocacy capacity. The Steering Committee meets on a quarterly basis, while workgroups convene conference calls as needed. NCET holds its annual meetings in conjunction with partner conferences.

NCET has created several publications. The *Federal Funding Gap Report* is an update to the 2002 report to Congress developed in response to the IOM report on TB. The primary audience of the document was U.S. Congressional staff, but the report was also distributed to ACET, NCET and the media. *TB Elimination: An Advocates Guide* is used as a tool during NCET's TB advocacy training sessions, but groups can obtain additional assistance from NCET in this area. The *NCET Wire* is a quarterly electronic publication that contains information on TB funding and leadership issues; ongoing activities by NCET and its partners; new educational products; and key points from ACET, ATS and other TB-related meetings. All ACET members are on the e-mail distribution list to receive the *NCET Wire*. TB-related news items reported in the media are summarized and circulated on a quarterly basis. Additional information on NCET can be obtained from 202/494-2448 or jseggerson@tbcoalition.com.

ACET commended NCET on developing and circulating TB publications. Both the *NCET Wire* and *Federal Funding Gap Report* provide extremely useful information on the current status and future direction of TB control and elimination.

Update on the Respiratory Protection for Airborne Infectious Agents (AIAs) Stakeholders' Workshop

Dr. Adelisa Panlilio, of the CDC Division of Healthcare Quality Promotion (DHQP), provided a status report on the meeting. Dr. Dixie Snider, the CDC Associate Director for Science, established and charged a workgroup with planning the workshop. The workgroup is represented by DTBE, DHQP, the National Institute for Occupational Safety and Health (NIOSH), and Office of Terrorism Preparedness and Emergency Response (OTPER). A representative of the Occupational Safety and Health Administration (OSHA) serves on the workgroup as a liaison member.

The workgroup has held weekly conference calls since August 2004 and has reserved meeting space with capacity for 300-500 persons. The workshop is a CDC activity and the current plan is to convene on November 30-December 1, 2004 in Atlanta with three major objectives. First, current scientific knowledge of the transmission of selected AIAs and respiratory protection for AIAs will be discussed. Second, strategies to improve the quality of respiratory protection will be explored. Third, critical research and "policy" needs will be identified and a time-line will be developed to address these needs.

The workshop is not intended to influence or change OSHA's respiratory protection policies and regulations. Instead, CDC will make efforts to develop a research agenda that identifies data gaps in transmission and respiratory protection of AIAs and create a guidance document on respiratory protection. Speakers and moderators for the workshop will be current and former CDC staff who are still being identified at this time, but a draft agenda has been developed. On November 30, 2004, CDC and OSHA leadership will make opening remarks. Four major presentations will cover basic information on AIA control; current knowledge of TB, smallpox and severe acute respiratory syndrome (SARS); current science on respiratory protection; and research on respiratory performance.

On December 1, 2004, perspectives and outlooks will be provided by three groups: OSHA and international regulatory agencies; respiratory manufacturers; and respiratory users in hospital, infection control, occupational health and industrial hygiene settings. The possibility of adding another session to briefly present and discuss liability issues is being considered. A discussion period will be opened to identify gaps in research and guidance. The workshop will soon be announced in the *Federal Register*.

ACET pointed out that the workshop will be useful for gathering state-of-the-art data, but will most likely not be helpful to field staff who are charged with responding to OSHA's new respiratory protection regulations. The draft agenda is weighted with didactic

presentations and a reiteration of extant data on respirators. However, the original intent of the workshop was to convene experts to respond to stakeholders' questions on respiratory protection and develop evidence-based guidelines for appropriate selection and use of respiratory protection in healthcare facilities. The draft agenda does not provide an opportunity for infection control and prevention stakeholders to engage in meaningful dialogue, link data to actual clinical practice in healthcare facilities and reach consensus on this issue.

Professional societies and other stakeholders that strongly advocated for CDC to hold the workshop are extremely concerned because the draft agenda does not reflect the original goal. Moreover, CDC has not clearly defined the outcomes of the meeting. ACET urged the planning workgroup to revise the agenda for CDC to obtain diverse perspectives during the workshop rather than make presentations. This goal could be achieved with several approaches. For example, the number of presentations could be shortened if stakeholders were given published data on respiratory protection for AIAs prior to the meeting. Breakout sessions could be held with smaller groups that would be charged with discussing specific topics and reporting key findings to the full workshop. The participants could then identify a few critical areas that overlap all respiratory agents. ACET requested that these concerns be communicated to Dr. Snider.

ACET expressed another concern related to this issue. John Henshaw, Assistant Secretary of Labor for OSHA, misquoted ACET's position on respiratory protection regulations in a recent Washington Post editorial. The article inaccurately suggested that ACET supports OSHA's enforcement of the General Industry Respiratory Protection Standard. During a conference call with his staff and Dr. Kawamura, Secretary Henshaw confirmed that he understood ACET's perspective and will not misrepresent these views in the future. Secretary Henshaw asked to meet with Dr. Kawamura and other ACET members in person prior to the stakeholders' workshop. The meeting will provide a solid opportunity for ACET to continue dialogue with OSHA.

CDC made follow-up remarks to ACET's comments. Efforts will be made during the open discussion period to maximize dialogue, but the presentations will be critical due to the diversity of respiratory protection knowledge among stakeholders. The presentations will also be necessary because reuse of respirators, regulatory perspectives and other complex technical issues warrant close examination. The planning workgroup is considering the possibility of convening conference calls with the speakers before the workshop to identify relevant information to present and important questions to address during each session. The planning workgroup has also prepared guidelines to produce an extended abstract with bibliographic materials. If time permits, these documents will be compiled and posted on a web site prior to the workshop and also assembled in notebooks for distribution during the meeting.

During the meeting of the Healthcare Infection Control Practices Advisory Committee on October 4-5, 2004, CDC asked the members to submit relevant issues that should be discussed during the workshop. ACET should explore the possibility of taking this action as well. Dr. Julie Gerberding, the CDC Director, and Secretary Henshaw have agreed to thoroughly review recommendations and other key outcomes from the workshop and engage in further dialogue to identify next steps.

ACET concluded the discussion with general agreement to take the following actions. The members will provide Dr. Kawamura with a list of relevant TB issues to discuss during the workshop and important outcomes to consider. The members will submit these comments to Dr. Kawamura before the meeting adjourns on the following day. Dr. Kawamura will contact Dr. Snider by telephone and in writing to discuss ACET's comments. She will also communicate ACET's concerns by posing five key questions to Dr. Snider.

One, what is the outcome of the workshop? Two, what is the process for follow-up and accountability of issues decided at the workshop? Three, what is the process for participants to provide comments and make recommendations? Four, how will the workshop advance various infection control guidelines? Five, is the purpose of the workshop to advise CDC or build consensus among participants to make recommendations? Dr. Kawamura will revise the questions to reflect the Executive Secretary's clarification that the workshop will not be convened for the participants to reach consensus in accordance with FACA rules. CDC agreed to notify ACET by e-mail when the workshop is announced in the *Federal Register*.

Update on the Draft ATS/CDC/Infectious Disease Society of America (IDSA) TB Control Guidelines

Dr. Charles Nolan served as the ATS co-chair for the committee that revised the 1992 statement on TB control in the United States. The 19-member writing committee also had CDC and IDSA co-chairs; several members representing the three organizations; three expert reviewers; and formal representation by NTCA, the American Academy of Pediatrics and Canadian Thoracic Society. Dr. Nolan outlined the background and current status of the document. ATS, CDC and IDSA revised the 1992 TB control statement due to the changing epidemiology of TB. In the 1990s, new workers and investigators were attracted to the TB control field; new funding sources emerged; the United States became involved in the global TB epidemic for the first time; and interest in TB elimination in the United States was rekindled.

Revived interest in TB stemmed from a successful national control effort. In the early 1990s, a virulent resurgence of TB occurred, MDR-TB transmission and nosocomial transmission of TB were virtually eliminated, and TB incidence declined for 11 consecutive years. Less than 15,000 TB cases were reported in the United States in 2003 compared to >28,000 cases in 1992, but current evidence suggests that this decline may not continue. No progress has been made in TB among foreign-born persons; advances have not been made in TB in low-incidence areas; and the rate of decline in TB incidence has decreased in recent years throughout the country. The trend in the decrease over the past several years is changing compared to the slope of the decline over the past nine years.

ATS, CDC and IDSA periodically issued guidelines for TB diagnosis, management and control. Three of the four statements were revised in 2000-2003, but the 1992 TB control guidelines had never been updated prior to this effort. The writing committee revised the statement in 2001-2003, distributed the draft for internal and ATS review in 2003-2004, and is now awaiting approval from the CDC cross-clearance process. The revised statement is expected to be published in early 2005. The writing committee acknowledges that the two-year period to revise the statement was long and the document is quite lengthy with 225 pages and 438 references. However, the writing committee was committed to presenting evidence-based recommendations and updating the guidance on high-risk groups and settings. Moreover, much time has passed since the previous TB control statement was published.

The revised TB control statement features several new areas. First, the document links TB control to progress toward TB elimination and identifies the five most significant challenges in this effort. TB persists among foreign-born persons residing in the United States. Delays are associated with detecting and reporting new TB cases. Capacity to protect new contacts of infectious TB cases and respond to TB outbreaks is not optimal. The large reservoir of 10-15 million persons in the United States with LTBI persists. Maintaining clinical and public health expertise in an era of declining TB incidence is difficult.

Second, the document expands basic TB control principles from three to four. TB cases must be promptly detected, reported and treated. Contacts of infectious TB cases must be evaluated and protected. TB must be prevented among persons with LTBI who are at risk of progressing to active TB. Transmission of TB must be prevented in healthcare facilities, correctional institutions, homeless shelters and other high-risk settings. Availability of solid smear microscopy and capacity for rapid turnaround of TB results are at the core of case detection.

Third, the document emphasizes the need to improve case detection and strengthen private/public health partnerships. This strategy will increase the likelihood that TB

cases will be cured, contacts will be protected and transmission will be prevented. For example, a person with respiratory symptoms will seek care from a healthcare provider, but will face social, economic and cultural factors that impact access to and knowledge of the need for care. The healthcare provider will have knowledge, training and skills to treat the patient and will also have access to consultant and laboratory services. Factors from both the patient and provider perspectives must be considered before a TB case can be diagnosed, reported and treated.

Fourth, the document outlines a new paradigm for targeted testing and LTBI treatment; describes a new approach to identify populations at risk for TB infection; and identifies roles and responsibilities in TB control and elimination efforts outside the public health sector. The traditional model of TB control in the United States is no longer optimal during a sustained drive toward elimination because planning and executing this approach almost exclusively reside with the public health sector. Success in TB elimination in the United States will depend on integrated activities of professionals from diverse health science fields.

Specific roles should be assigned to pediatricians and other private medical practitioners, civil surgeons, community-based clinics and organizations, hospitals, academic institutions, medical professional organizations, correctional facilities, biotechnology industries and pharmaceutical companies. For example, medical societies can play a role in TB control efforts by providing professional leadership on clinical practice and TB control; educating and training members and other health professionals in TB diagnosis, treatment, prevention and control; advocating for TB control and research; and promoting greater U.S. involvement in global TB control efforts.

Fifth, the document identifies unmet needs to improve TB control and progress toward TB elimination. Enhanced strategies to diagnose and treat LTBI would impact three major challenges to continued progress. Studies on the changing epidemiology of TB in the United States should continue. Many fundamental approaches to TB control lack an established scientific basis. For example, the “high-risk” subgroup within the foreign-born population has not been identified. State and local programs should identify high-risk persons by strengthening knowledge of the epidemiology of TB in local jurisdictions. A group of experts should be convened to discuss this issue in more detail. Exposures that constitute a contact have not been clearly defined. Strategies to remove *M. tuberculosis* (*M.tb*) from ambient air and evaluate TB programs have not been developed.

Dr. Nolan provided additional details about the revised TB control statement in response to ACET’s questions. Management of individual cases is not discussed since this issue is extensively covered in the 2003 ATS/CDC/IDSA TB treatment guidelines. However,

the document outlines responsibilities of health agencies to conduct case management and also recommends including cohort reviews as a key component of program evaluation. The document contains assumptions about the risk of LTBI with respect to contacts, but the contribution of LTBI treatment to effective TB control is not described because no solid data have been produced to demonstrate this impact.

Update on Improving Global TB/HIV Collaborative Activities

Dr. Reuben Granich of DTBE provided a status report on ongoing efforts to integrate global TB and HIV programs. Between 35-40 million persons are infected with HIV worldwide, but Africa is most heavily impacted by the pandemic. The life expectancy in selected African countries with a high HIV prevalence has markedly decreased due to a widening treatment gap. AIDS deaths in the United States and Western Europe declined after ARV drugs were introduced in the mid-1990s, but mortality in Africa continued to increase. HIV is also changing the epidemiology of TB at the global level, particularly astronomical TB case rates reported in Botswana, Malawi, Tanzania and Zimbabwe.

CDC's efforts to support global AIDS initiatives since the 1980s include conducting HIV/AIDS research in Africa and Asia, establishing the Leadership in Fighting the Epidemic Initiative, funding GAP, initiating the President's International Mother and Child HIV Prevention Initiative, and participating in President's Emergency Plan for AIDS Relief (PEPFAR). Under PEPFAR, $15 billion will be allocated over five years to prevent 7 million new HIV infections, treat 2 million HIV-infected persons, and provide care to 10 million HIV-infected persons. The 15 focus countries include Africa, Haiti, Guyana and Vietnam. Since PEPFAR was launched in 2003, high-level ministers and other country leaders have been publicly tested for HIV to increase recognition of the problem.

International TB control efforts feature a five-point strategy of government commitment, case detection by sputum-smear microscopy, a standardized treatment regimen with directly observed therapy, a regular supply of anti-TB drugs, and a standardized recording and reporting system. The core elements of a TB surveillance system include estimates of TB incidence and prevalence, a patient registration system, cohort analysis with standard outcomes, and quality assurance. A program can use three documents for quality assurance. A TB register is a central document that is typically held at a district and contains the name of each person diagnosed with TB. A laboratory register documents screening by smear microscopy for TB. A treatment card is a record of each individual's personal TB treatment. Overseas programs use a cohort analysis to review outcomes and determine performance.

A basic TB surveillance program includes the following components. A peripheral health facility typically serves 5,000-10,000 persons, uses a patient treatment card and laboratory register, and produces a monthly report. A TB unit receives the monthly report and records all patients into a TB register. The district TB center conducts a cohort analysis, generates a quarterly report, and submits the document to a state TB cell and central TB division. The TB center in India contains four treatment units and 23 microscopy centers due to its large district of ~2 million persons.

Several efforts are underway to link HIV and TB programs. WHO developed an interim policy on collaborative TB/HIV activities in 2004 that called for the establishment of collaborative mechanisms, a decrease in the burden of TB in persons living with HIV/AIDS, and a reduction in the burden of HIV in TB patients. WHO also released guidelines in 2004 to emphasize the need for TB programs to conduct routine HIV surveillance among TB patients. The majority of HIV testing in heavily impacted countries was primarily a voluntary testing and counseling strategy in which individuals were required to self-identify their status and present to a stand-alone center for HIV testing and counseling. However, this paradigm has shifted to particularly address issues related to confidentiality and stigma.

UNAIDS produced a groundbreaking policy statement in June 2004 that called for HIV testing of all TB patients as a part of routine management. The policy will facilitate an "opt-out" strategy in which patients who are diagnosed with TB will be offered HIV testing, but can refuse the test. The new TB/HIV surveillance initiative is expected to benefit other areas as well. Progress can be tracked in testing TB patients for HIV, distributing core care packages to patients and performing other management functions. Case detection, conversion, default, death and other standard TB program indicators can be monitored. Access to care and treatment for TB patients with HIV/AIDS can be expanded with access to ARV drugs and provision of a core prevention and care package.

One of the most significant contributions TB programs will make to HIV/AIDS programs is the prompt analysis and feedback model that is used to document patient care and improve program performance. For example, DTBE produced a quarterly report with a cohort analysis and indicators for the India TB center and distributed the document directly to districts for feedback. DTBE attended quarterly review meetings, directly supervised the TB program, generated an annual report and developed a WHO global report. The new TB/HIV surveillance initiative will be based on the 2004 WHO guidelines and supported by PEPFAR funds. U.S. government agencies, WHO and several other partners are involved in the effort. The initiative will focus on countries with generalized HIV epidemics.

Several activities have been proposed for the TB/HIV surveillance initiative. Routine HIV testing for TB patients will be expanded; paper and electronic TB surveillance systems will be modified; technical assistance will be provided; and experiences will be shared to scale-up activities. CDC has taken initial steps to support the initiative. A meeting was convened in June 2004 with international stakeholders and TB program managers to establish a framework for activities, review current HIV and TB surveillance systems and discuss a collaborative approach. A workshop was held in Addis in September 2004 with international managers of TB and HIV/AIDS programs to develop joint action plans for HIV testing of TB patients. Both DTBE and GAP have assigned staff to lead the initiative.

DTBE acknowledges that several challenges will need to be addressed to successfully implement the TB/HIV surveillance initiative. Convening national TB and HIV/AIDS programs to discuss roles and responsibilities will be difficult due to historical distrust between the two groups and reluctance to partner. Staff to conduct TB/HIV collaborative activities are extremely limited. The new initiative may weaken TB control if additional resources are not allocated. Stakeholders must endorse changes in TB surveillance systems to include HIV.

Programs must address concerns related to ethics, stigma and confidentiality. Issues need to be resolved on whether TB or HIV/AIDS programs will administer drugs to patients with TB/HIV coinfection. TB programs can play a significant role in this effort by informing policymakers that even in the absence of ARV drugs, treatment of opportunistic infections is extremely beneficial from a public health perspective. Most notably, patients who begin TB treatment are being prepared for ARV delivery. Both programs will need to expand beyond traditional strategies. For example, HIV/AIDS programs should provide LTBI treatment to persons with TB/HIV confection because the TB latency period is much shorter in HIV-infected persons.

Efforts are underway to address this issue. Many HIV/AIDS programs are shifting to a community model in which HIV testing is administered in homes and individuals are evaluated for TB and a variety of other diseases. HIV/AIDS programs must also focus on TB contact investigations, particularly for children and parents. TB programs should continue to manage smear-positive persons, but should place more emphasis on smear-negative persons since these cases are a major issue for HIV. Despite these challenges, CDC was pleased that TB/HIV collaborations have already shown benefits. The TB program in India partnered with the national AIDS programs to identify persons with TB/HIV confection. Preliminary data showed that the number of cases detected increased by ~5%-10%.

ACET was concerned that the new TB/HIV surveillance initiative will only focus on TB/HIV confection. This approach will not be effective in preventing additional TB cases

because TB contacts who eventually develop TB will not be detected. ACET encouraged CDC to place more emphasis on Asia and China due to the HIV epidemic in these countries. Aggressive efforts should be made to address TB in Asia and China before these populations migrate to the United States.

CDC announced that the Gates Foundation will award a large grant to several countries to develop strategies to accelerate the decline of the TB epidemic. One of these activities will focus on contact tracing in Zambia. The Stop TB Partnership plans to discuss the HIV epidemic in China and TB/HIV collaborations during the meeting of its coordinating board in Beijing, China in October 2004. CDC has a presence in China through GAP.

Synergy and Collaboration Between TB and Public Health Preparedness (PHP) Programs

Federal Perspective. Mr. Charles Schable, the Office of Terrorism Preparedness and Emergency Response (OTPER) Director, described collaborative efforts the TB and PHP fields can undertake from CDC's perspective. He was pleased to announce that the "full-use" concept of applying federal PHP dollars to other activities is gaining acceptance. For example, the NTCA web site contains an excellent overview of areas where TB and PHP can assist the other field and also describes mechanisms to use PHP funds to hire communicable disease investigators. TB program staff have a wealth of experience and knowledge to contribute to PHP, including expertise with an aerosol-transmitted disease, isolation procedures, quarantine regulations, management of large identification programs and transportation of infected patients. As a result, TB program staff should be consulted and extensively involved in state and local PHP meetings and other planning procedures for any event.

State Perspective. Dr. Sarah Royce is a TB controller in the California Department of Health Services (CDHS). She described a TB case study in California and TB efforts to illustrate areas where federal agencies can foster TB/PHP synergy. A Hmong refugee 41 years of age arrived in the United States with infectious TB in June 2004, but was diagnosed with bladder cancer in Thailand in 2003 and cleared for travel in April 2004 based on an immigration examination by a panel physician and a normal chest x-ray. The patient was hospitalized in May 2004 in Thailand due to cavitary disease, but his smear-positive sputum converted to smear-negative during the course of TB therapy. Upon U.S. arrival, the patient was transported to a Sacramento hospital and found to be smear-positive based on cavitary chest film. The patient died eight days after arriving in the United States in June 2004 and was found to have MDR-TB based on a postmortem review of his isolates in July 2004.

CDHS implemented a table-top exercise to determine gaps in the public health system that allowed an infectious TB patient to enter the United States. This activity identified problems in four major areas: the quality assurance process of overseas panel physicians conducting immigration examinations; the TB treatment program in Thailand; case detection by the Los Angeles quarantine station of an arriving passenger who was ill; and coordination across agencies and organizations at international, federal, state and local levels. CDHS was extremely concerned about the case because current flaws in the public health system may allow U.S. entry to an individual with an unknown pathogen who was not required to undergo screening at a U.S. quarantine station or overseas.

Based on 2003 data, California reported the most new TB and MDR-TB cases of any state. Texas and New York had the second and third highest number of new TB cases, respectively, and collectively reported 3,071 cases in 2003. However, 3,227 new TB cases reported by California in 2003 were more than those two states combined. The 2003 TB data can also be used as an indicator to demonstrate that states are unprepared. California, New York and Texas saw increases in TB cases, while the nation experienced the smallest decrease in U.S. TB cases in more than ten years. MDR-TB continues to be imported from legal and undocumented immigrants; TB continues to develop in the United States when treatment is inadequate; and TB transmission and MDR-TB outbreaks are ongoing.

Because new bioterrorism (BT) dollars are the largest awards in U.S. history, attention on the critical importance of strengthening the nation's public health infrastructure has never been more focused. In 2002, CDC and other federal officials urged the United States to use this unprecedented opportunity to strengthen public health by building core capacity to deliver essential public health services. The TB community has taken several actions to take advantage of BT funding. NTCA developed a series of discussion papers to describe areas where TB programs can contribute to PHP; outline strategies for PHP to enhance the basic TB infrastructure, and identify key and cost-effective approaches to use communicable disease investigators in PHP.

CDC's 2004 BT program announcement required that funds be used to upgrade preparedness of state and local public health jurisdictions in responding to BT, infectious disease outbreaks, public health threats and emergencies. The program announcement expanded "BT preparedness" to an "all-hazards" approach and "full use" of resources, but the language continues to be controversial to states and local areas and should be more clearly defined. To assist in this effort, NTCA administered a qualitative survey in September 2004 to TB controllers in 24 states and four cities. The survey focused on the TB/PHP interaction, TB's contribution to PHP, and the impact of PHP on TB. To date, six of 12 states with high TB case rates and 18 of 38 states with

TB case rates below the national average have responded to the survey. The results are outlined below.

For preparedness planning and readiness assessment, TB programs lent a significant amount of time and expertise to overseeing outbreaks and contact investigations; responding, planning and training for SARS; developing respiratory protection programs; planning the distribution of medications; reviewing grant applications; identifying and assessing airborne infection isolation rooms, updating quarantine and legal orders; and participating in PHP drills and planning exercises. TB programs benefited from the last three activities. For surveillance and epidemiological capacity, TB programs contributed by staffing command centers, regional field offices, and emergency response teams and shelters. TB programs benefited from augmented regional field, administrative and medical staff and the "career ladder" for field investigators.

For laboratory capacity, TB programs provided a model of a regionalized system of surge capacity to ensure that TB testing is routed to regional laboratories and state laboratories are free to address BT agents. TB programs benefited from laboratory upgrades. For health alert networks, information technology, risk communication and dissemination of health information, TB programs benefited from web-based reporting, patient management systems, additional computers, mass facsimiles to community providers about persons with TB signs or symptoms, and improved linkages to infection control practitioners and public health facilities at district, county and local levels.

For education and training, TB programs provided training in the areas of contact investigation, epidemiology and outbreak containment and also cross-trained staff in emergency surge capacity. TB programs benefited from PHP field investigators who were cross-trained in TB to develop and maintain skills and community networks. Overall, the survey demonstrated that TB programs provided expertise and time, while PHP programs bolstered the case for TB control, improved linkages within public health and the broader community, and funded equipment, staff, training and information systems.

The survey also identified key factors that facilitate TB/PHP collaboration. Organizations should be located in the same division or entity, assign the same staff to TB and PHP activities, and have strong partnerships with regional health departments. PHP programs should recognize the expertise of other groups, welcome input and offer compensation. TB programs should be invited to fully participate in all PHP initiatives and PHP funding should be increased. Survey respondents noted several barriers to TB/PHP collaboration as well. On the one hand, PHP expects TB to lend its expertise to BT to promote national security, but is unwilling to allocate any categorical BT dollars

to TB. On the other hand, TB is understaffed and does not receive sufficient compensation to lend its staff and other expertise to PHP.

Overall, TB controllers found the PHP collaboration to be a detriment to TB programs because BT is viewed as more important than TB; BT is a tremendous distraction from routine TB activities; and the most experienced TB staff are given incentives to transfer to BT. A 2004 article published in *Health Affairs* described lessons California learned about local variations in PHP. The article acknowledged the need to remain vigilant for potential unintended consequences because several years will pass before the consequences of recent preparedness investments create public health emergencies.

Despite these challenges, a critical need exists to identify opportunities for synergy between TB and PHP. TB continues to be a public health threat, particularly since MDR-TB is classified as a category C agent. Existing capacity should be expanded to be more efficient and effective instead of taking a traditional siloed approach. Making investments to one public health program to the detriment of another is counterproductive. This strategy will cause the United States to be less prepared for both well-known and new threats. NTCA has made several recommendations to foster TB/PHP synergy. Federal agencies should clearly define and broadly disseminate "full-use" funding and "audit disallowances" to all PHP programs. TB/PHP collaborations should be structured into grant requirements. The impact of PHP funds on the public health system should be formally evaluated and reported. Performance measures should be developed and implemented.

DTBE should proactively identify opportunities, facilitate efforts at the national level, and distribute specific tasks to the field for action. For example, several states have taken advantage of BT dollars awarded by the Health Resources and Services Administration (HRSA) for hospital isolation capacity. Training centers and border initiatives also present opportunities for TB/PHP synergy. BT dollars proposed for FY'04 and FY'05 will place more physicians, epidemiologists and information systems personnel in quarantine stations. If these multi-disciplinary teams will be truly established to respond to health emergencies, monitor and enforce requirements for travelers and communicate disease intelligence to partners, capacity to control TB will be tremendously enhanced.

ACET extensively discussed NTCA's recommendations for TB/PHP collaboration and synergy. Participation of TB controllers in BT table-top meetings and exercises detracts from daily TB activities. The involvement of TB programs in PHP initiatives will cause infection and TB control efforts to be neglected in the future. ACET suggested other actions that can be taken to foster synergy between the two fields. PHP staff should be trained in acid-fast bacillus (AFB) smear and gram stain screening. Grant administrators should be more flexible in allocating PHP dollars to state TB programs.

Development and implementation of solid performance measures should be prioritized as a critical need in TB/PHP collaboration. TB and PHP programs should place more emphasis on prevention, identification and quarantine of agents during an event since TB is a biological agent that can be easily handled with personal protective equipment. Efforts should be made to link to existing initiatives. For example, the Association of Public Health Laboratories (APHL) has established a TB steering committee to review gaps in current laboratory capacity and attempt to resolve these problems.

ACET proposed that NTCA's recommendation for quarantine station expansion be broadened to include collaboration with U.S. Customs and Border Protection (CBP). Of the 300 ports of entry into the United States, only eight have quarantine stations. The revised language would highlight the need to improve detection of infectious diseases upon U.S. arrival and address existing gaps at ports of entry with no quarantine stations. For example, Border Patrol agents cannot leave a port of entry to transport infectious patients to a quarantine station or appropriate care facility. Moreover, Border Patrol agents are not public health professionals and have no training and skills to identify TB or other infectious diseases.

CDC made several remarks in response to ACET's discussion. Of CDC's $1.77 billion annual budget, 14% is allocated to BT. Of the BT budget, ~$1 billion is allocated to states each year. On the one hand, CDC recognizes that the strong focus on BT will cause continued shortages in the public health workforce and result in further neglect of TB, HIV, STDs and other important public health issues. For example, nearly six weeks passed between the time the Hmong refugee was hospitalized in California with infectious TB and CDHS detected MDR-TB. This delay demonstrates that laboratory capacity is insufficient to identify a class C agent despite the availability of technology for more rapid turnaround of results. On the other hand, TB programs must take caution in recommending that a more flexible strategy be applied to allocate categorical BT dollars. PHP will expect TB to share its resources as well. DTBE has attempted to address this concern by using BT funds to train TB staff in other disciplines.

CDC is attempting to interpret full-use funding to determine the extent to which BT dollars can be allocated to other areas, but Congress has not reached consensus on defining this term. CDC cannot release guidance to states on full-use funding without Congressional approval. However, the new five-year funding cycle of BT grants will begin in FY'05 and the language will be much more specific than previous years. Grant requirements are currently being written to completely eliminate focus areas, include performance indicators, and describe expectations for grantees to expand BT activities to include PHP initiatives. CDC is extensively soliciting input from external partners in developing performance indicators for state grantees.

CDC also made comments in response to NTCA's recommendations for TB/PHP synergy and collaboration. DTBE and the Division of Global Migration and Quarantine (DGMQ) hold monthly management meetings and have agreed to place the recommendation for quarantine station expansion on the November 2004 agenda. DTBE and DGMQ will then meet with TB controllers to discuss changes that must be made in the field. Congress has directed CDC to allocate a portion of BT dollars to establish 25 quarantine stations. CDC is partnering with the Department of Homeland Security (DHS) to resolve existing problems with U.S. ports of entry, particularly those with no quarantine stations.

ACET concluded the discussion with agreement to take the following actions. NTCA's recommendations for TB/PHP collaboration and synergy will be distributed to ACET for a more detailed review. ACET will take formal action on the recommendations on the following day.

HRSA TB Prevention and Control Resources

Overview. Dr. Theresa Watkins-Bryant is the ACET *ex officio* member for HRSA. She reported that HRSA's three primary goals are to expand access to high-quality and culturally-sensitive health care; improve health outcomes among minority communities in America; and prepare communities to treat victims of a BT attack. HRSA is organized into five bureaus and one office. The Bureau of Health Professions is a $937 million program that trains physicians, nurses and other providers and places these professionals in areas of most need. The HIV/AIDS Bureau (HAB) is a $2.05 billion program that provides life-saving medication, health care and support services to >530,000 low-income persons with HIV/AIDS. HAB awards HIV emergency relief project grants and provides funding to >600 Ryan White Comprehensive AIDS Resources Emergency Act (RWCA) grantees.

The Maternal and Child Health Bureau is a $1.01 billion program that partners with states to expand access to health care for >27 million women, infants and children. The Bureau of Primary Health Care is a $1.75 billion program that supports 3,600 health centers and clinics to deliver preventive and primary health care to ~12.5 million low-income and uninsured persons. The Healthcare Services Bureau is a $1.03 billion program that oversees the nation's transplant systems, assists communities in responding to mass casualty events and compensates families of children harmed by vaccines. The Office of Rural Health Policy is a $143 million program that awards grants and provides technical assistance to help rural healthcare providers build coordinated systems of care and improve access to medical services among local residents.

HRSA has a wealth of resources in addition to those housed in its office and bureaus. Most notably, the geospatial data warehouse (GDW) that was developed in March 2003 is an exciting web-based tool to place HRSA on a map and allow users to identify HRSA resources in a more efficient manner. GDW provides a single point of access to information; a visual illustration of HRSA resources throughout the United States and territories; and a repository of integrated health care services and other data from external sources for mapping and reporting analyses.

For example, programs and individual users in Fulton County, Georgia would access GDW and create maps to locate HRSA's investments in the area. These resources include Medicare rural hospitals, state rural health offices, trauma emergency medical services, healthcare facilities and National Health Service Corps providers. GDW can also be formatted to obtain more specific data elements, such as the names of grantees in each bureau, award amounts and ongoing projects. GDW data can be used in conjunction with the HRSA web site to obtain details about a particular bureau or program.

In addition to general information, GDW also provides specific details of relevance to a program or individual user. For example, primary healthcare grants would be of particular interest to the TB community because this funding supports the Healthy Community Access Program, health center clusters, integrated systems planning and clinical networks. A major focus of primary healthcare grants is to facilitate synergy among programs. DTBE could create a GDW map of primary healthcare grantees in Fort Wayne, Indiana, contact medical directors of the respective facilities, and emphasize the importance of establishing linkages with the health department. HRSA-funded health clinics and the health department could then jointly develop strategies to build local capacity in diagnosing and treating active TB and LTBI.

In addition to the overview, Dr. Watkins-Bryant also clarified common misconceptions about HRSA. Community health centers (CHCs) are housed in HRSA's Consolidated Health Center Program and are not an individual activity. This initiative accounts for <33% of HRSA's $7.2 billion annual budget. HAB is HRSA's only disease-specific program; all other funding is awarded to organizations to deliver comprehensive services to patients. HRSA grantees are expected to provide services based on current, state-of-the-art and evidence-based guidelines developed by CDC and the Agency for Healthcare Research and Quality.

HRSA conducts performance reviews to identify guidelines utilized by grantees and make recommendations to improve services. However, HRSA does not develop and implement prescriptive policies for organizations to deliver care. HRSA does not allocate TB-specific dollars, but its office, bureaus and other resources located throughout the country demonstrate that several opportunities exist for HRSA to

collaborate with DTBE and other TB partners. Additional details about HRSA can be obtained at www.hrsa.gov; GDW can be accessed at http://datawarehouse.hrsa.gov.

ACET made several remarks in response to the HRSA overview. GDW is a tremendous resource for the TB control community because programs now have a tool to easily locate HRSA resources at the local level. For example, the Washington State Department of Health (WSDH) created GDW maps to locate Migrant Health Clinics in the state. Staff were then assigned to conduct training on the Binational TB Card Project in each clinic. GDW has the potential to strengthen collaborations between health departments and CHCs in the future, but many TB programs have found that CHCs are reluctant to partner since TB is not included in HRSA's health disparities initiative. For example, the San Francisco Department of Public Health (SFDPH) has encountered significant difficulties in attempting to identify TB screening policies of the local CHC.

These barriers should not exist because TB programs and CHCs target the same populations. HRSA should include TB as an indicator while monitoring grantee compliance to guidelines. For example, HRSA performance evaluations should assess the degree to which CHCs adhere to TB recommendations established by CDC, states or local programs. Because resources in local TB programs have been severely cut, HRSA must include TB screening and LTBI treatment as primary care issues at the federal level. CHCs will continue to ignore TB without oversight and direction from a higher level. ACET acknowledged that barriers to collaboration between TB programs and CHCs can be minimized if TB programs offer incentives. Similar to TB programs, CHCs also face constraints with funding, personnel and other resources. For example, the Seattle TB program provided services to patients who were screened for TB by the local CHC at no cost, including chest x-rays, isoniazid, and consultation on drug hepatotoxicity and side effects.

Dr. Watkins-Bryant addressed ACET's comments as follows. HRSA is exploring the possibility of establishing a respiratory disease collaborative under its health disparities initiative that would include TB. However, internal challenges persist in emphasizing the importance of TB. HRSA continues to reiterate that its budget does not contain a line item for TB; its mission is to ensure patients receive comprehensive primary care services; and its grantees are responsible for providing TB care to individual patients.

HRSA's ability to require health centers to focus on TB is extremely limited because HRSA dollars only account for 25% of a grantee's funding. HRSA's oversight of health centers was further weakened during its recent reorganization. Field office clinicians now conduct performance reviews every five years and no longer make regular site visits to provide grantees with recommendations for improvement. As a result, the clinical presence has been eliminated from the field office and moved to a centralized

location. HRSA is exploring a number of strategies to ensure clinical performance reviews of grantees are not completely absorbed by the new organizational structure.

Dr. Watkins-Bryant proposed several action steps for ACET to consider to enhance HRSA's collaboration with the TB community. ACET should provide HRSA with concrete suggestions to advance the respiratory disease collaborative. ACET should provide HRSA with a list of additional TB indicators to include in HRSA performance reviews. Individual members should contact HRSA to describe barriers local health departments are facing in collaborating with CHCs and identify creative approaches to address these issues. For example, HRSA could facilitate conference calls with the TB controller and CHC medical director.

CDC agreed that several opportunities exist for HRSA to collaborate with the TB community. For example, the GDW web site can be featured in the next DTBE "Dear Colleague" letter to TB controllers to ensure TB programs are aware of local HRSA resources. A compelling argument, solid justification and other strong efforts can be made to emphasize the critical need to include TB in HRSA's health disparities initiative. Recent analyses of TB in the Southeast and urban cities can be summarized to illustrate this point.

HRSA previously addressed TB in its joint initiative with the CDC Division of Diabetes Translation. Lessons learned from this effort could be applied if HRSA is successful in establishing the respiratory disease collaborative. CDC also saw benefits in individual ACET members contacting HRSA to discuss barriers local health departments encounter while attempting to collaborate with CHCs. However, this activity could be expanded to produce more meaningful outcomes and generate information that is more representative of the United States. NTCA could administer a survey on CHC challenges to all TB controllers in its membership.

TB Services for HIV-Infected Persons. Ms. Suzanne Marks, an epidemiologist with the Health Systems Research Team of DTBE presented preliminary information on the collaborative project between DTBE and HRSA/HAB. The rationale for the project is as follows. At least 9% of 15,075 reported TB patients in 2002 and 15% of those 25-44 years of age were HIV-infected. HIV is the greatest known risk factor for TB disease after infection. Targeted TB screening and treatment of HIV-infected persons address priorities outlined in DTBE and DHAP strategic plans, the IOM report, DTBE's response to the IOM, and the Federal TB Task Force Plan. Current guidelines recommend tuberculin skin testing (TST) soon after an HIV diagnosis; LTBI treatment for HIV-infected persons with TST reactions $\geq$5 mm; and annual TST for TST-negative HIV-infected persons who are at risk for TB exposure or have experienced immune reconstitution.

The literature describes two major multi-site studies in the United States of TB screening among HIV-infected persons. The first study used the HIV/AIDS reporting system to select patient's records at three U.S. sites, review medical records and determine whether patients were screened for TB. In a cohort of 869 persons, the average time from HIV diagnosis to TST was six months; 54% received TST; 7% were TST-positive; and 41% did not receive LTBI treatment. The second study used the Supplemental HIV/AIDS Surveillance System (SHAS) that was implemented in 12 states. In a cohort of 11,396 persons, the average time from HIV diagnosis to TST was up to six or more years; 80% received TST; 8% were TST-positive; and 27% did not receive LTBI treatment. Neither of the studies validated completion of LTBI treatment. Findings from both studies indicated that implementation of LTBI treatment is less than optimal and emphasized the need to improve prevention in this high-risk population.

HAB's RWCA grantees provide care to ~500,000 persons per year. This population accounts for ~75% of HIV-infected persons who know their HIV status. Individuals who receive services from RWCA-funded providers are likely to be uninsured, under-insured or on Medicaid and at high risk for TB due to poverty. The overall goal of the DTBE/HAB collaborative project is to reduce TB incidence among persons living with HIV/AIDS by facilitating improvement in detection and treatment of TB and LTBI. The project was launched in August 2003 and will continue until September 2006 in two phases.

In phase 1 of the project, HRSA/HAB and HRSA-funded HIV clinics will be evaluated to identify written polices to provide TB services, TB screening and treatment rates, and providers who achieved high rates of TB diagnosis and treatment. In August 2003, DTBE and HAB established a memorandum of understanding (MOU) to share data and resources. In December 2003, DTBE interviewed HRSA headquarters staff about TB services, policies, procedures and reporting; and, throughout spring of 2004 collected written TB policies, procedures and training curricula from reporting HRSA grantees.

All RWCA grantees are required to report standardized data and submit CARE Act data reports (CADR) to HRSA. CADR forms contain a section for each provider to report aggregate data on unduplicated HIV-infected clients who received TST, were treated for being TST-positive, or diagnosed with active TB. In 2005, HRSA plans to modify the TB elements on CADR forms to include treatment completion and improve denominators. DTBE is currently analyzing 2002 CADR data.

In phase 2 of the project, case study research will be conducted at six clinics in three cities with high TB/HIV prevalence to identify how grantees successfully provide TB prevention services; characteristics and activities associated with high rates of TB screening and treatment; and costs to society and HIV programs to conduct TB screening and treatment. At each of the six clinics, key staff will be interviewed; data

reported to HRSA and a random sample of 150 patient charts will be analyzed; two focus groups will be held with clients; written policies and protocols will be collected; clinic activities will be observed; and cost data will be gathered. DTBE and HAB will agree upon methods and formats to disseminate findings.

Major output indicators of the case studies will be rates of LTBI diagnosis and treatment and factors associated with higher rates. TB policies and procedures, referral networks, education, client perceptions, diagnosis and treatment costs per client, and costs per case and death prevented will be described as well. To date, DTBE and HAB have developed data collection instruments, selected the three cities and discussed study methods. DTBE and HAB plan to select the six clinics in November 2004, issue contracts and obtain approval from an Institutional Review Board (IRB). DTBE and HAB expect to pilot the study at the first site in March 2005.

Overall, HRSA's access to this high-risk population will provide an opportunity to prevent TB morbidity and mortality and improve services. The collaborative project addresses priorities identified by CDC, HRSA, IOM and the Federal TB Task Force (FTBTF). This initiative will also facilitate evaluation of an important program and establish a framework for future collaborations.

With no further discussion or business brought before ACET, Dr. Kawamura recessed the meeting at 4:08 p.m. on October 6, 2004.

Current ACET Business

Dr. Kawamura reconvened the meeting at 8:45 a.m. on October 7, 2004 and opened the floor for announcements and reports on outstanding agenda items. DTBE distributed OMH's proposal to the Advisory Committee to the CDC Director as requested by ACET on the previous day. Five vacant positions for CDC center directors will be open for competition to both external and internal candidates within the next week. ACET was encouraged to nominate persons with a commitment to and history in TB control for the position of the NCHSTP Director.

A meeting will be held on December 6-7, 2004 with the TB and infection control workgroup that was established to update the 1996 guidelines for TB prevention and control in correctional facilities. The workgroup members will provide status reports on revisions to their respective chapters during the meeting. ACET members who have an interest in reviewing the drafts should notify DTBE. DTBE will seek permission from ATS and IDSA to distribute the draft TB control statement to ACET at this time since the document is not yet publicly available. DTBE will circulate an e-mail to advise ACET of the decision.

Dr. Kawamura entertained a motion to accept the previous meeting minutes; the motion was properly made and seconded by voting members. The June 23-24, 2004 ACET Meeting Minutes were unanimously approved with no changes or further discussion.

Dr. Kawamura provided an update on ACET's June and October 2004 letters requesting that the HHS Secretary add TB to the health disparities list for minorities and meet with ACET to discuss the TB funding gap. Drs. Castro, Kawamura and Valdiserri met with Admiral Richard Walling, Director of the Office of the Americas and Middle East, the Chief Pharmacist's Officer for the Public Health System, and Senior Advisor to the Surgeon General. Admiral Walling reports directly to Dr. William Steiger, Director of the Office of Global Health Affairs; Dr. Steiger reports directly to the HHS Secretary. Admiral Walling has extensive knowledge of TB and represents HHS on Ten Against Tuberculosis (TATB) and the U.S.-Mexico Border Health Commission (BHC).

The purpose of the meeting was to discuss ACET's high-priority issues, outline the current status of TB control, and obtain advice, support and a champion in HHS. ACET's request to add TB to the health disparities list and its concern about the TB funding gap were the major areas of discussion. NCET's federal funding gap report was referenced throughout the meeting. Other key points raised during the meeting are as follows. TB control has not been established for all groups. New strategies, research and technologies cannot be implemented to make further progress toward TB elimination without additional funding. Outcomes from the consultation on TB in the Southeast and the *MMWR* article on racial disparities were presented to emphasize that TB is indeed a health disparity.

TB rates are high among minorities and immigrants, but the disease has not been incorporated into the public health infrastructure or included as a primary care issue for minorities and under-served communities. Strong efforts have been made to address TB in foreign-born persons, particularly since 25% of cases are from Mexico. Border Health Commission (BHC) is represented on ACET and TATB has formulated a strategic plan for TB along the border. The Division of Immigration Health Services (DIHS) has developed a new process for persons diagnosed with active TB and detained by the U.S. Immigration and Customs Enforcement (ICE) to receive continued care.

The smear status of immigrants is known upon arrival in the United States, but the culture status is unknown because this capacity does not exist overseas. TB is the leading cause of mortality in AIDS patients globally, but AIDS receives more media attention and funding than TB in GAP. The TB community can play a significant role in PHP programs. The meeting concluded with the proposal of several action steps.

Admiral Walling suggested that Dr. Kawamura:

- Serve as a TATB liaison member.
- Review the TB section of the Surgeon General's global health report and call to action.
- Highlight key points from ACET's discussion on TB/PHP collaboration and synergy and submit the summary to Admiral Walling.
- Solicit new partners, particularly professional organizations of pharmacists.
- Forward an electronic copy of the NCET federal funding gap report to Admiral Walling.

Admiral Walling indicated that he would:

- Attend ACET's February 2005 meeting to present and discuss the TATB strategic plan.
- Determine the process within HHS to add TB to the health disparities list and provide a status report to ACET.
- Discuss ACET's summary of TB/PHP synergy and collaboration with the HHS Assistant Secretary for Emergency Preparedness.
- Provide ACET with contact information for professional organizations of pharmacists.
- Ask BHC to convene a summit of key stakeholders to discuss legislative policies that can improve TB control along the border and potentially leverage additional dollars.

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Dr. Kawamura entertained a motion to approve ACET's "10/6/04 draft" recommendations on TB/PHP synergy and collaboration; the document is appended to the minutes as Attachment A. However, several members outlined reasons to table the vote at this time.

- Distribute the draft to DGMQ for review, comment and clarification, particularly the request to "make full use of the quarantine station expansion."
- Specifically mention TB in the MOU DGMQ and DHS are developing to outline roles and responsibilities in the quarantine station expansion.
- Acknowledge that some communities currently have capacity to rapidly respond to TB and other BT agents since BT grants require states to develop laboratory response networks.
- Clarify request 2 to "structure collaboration into required recipient activities for all cooperative agreements" because the language is vague, generic and does not focus on a specific CDC cooperative agreement.

- Add the following language as request 7: "Act to identify and address regulatory and other obstacles to far wider availability and utilization of diagnostic microscopy at the point of patient contact."
- Revise the second sentence in the first full paragraph as follows to accurately reflect agency names and other terminology: "Specifically, ACET commends the interagency workgroup between the Department of Health and Human Services, Department of Homeland Security and U.S. Customs and Border Protection and encourages the inclusion of TB activities in coordinating multi-disciplinary teams at ports of entry and/or Border Patrol stations.

A motion was properly made and seconded by voting members for ACET to revise and submit specific recommendations to CDC to optimize TB/PHP synergy and collaboration. **The motion was unanimously approved.**

ACET agreed to take the following action steps. Dr. Flood, Dr. Kawamura and Ms. Napolitano will serve on a workgroup to obtain input and revise the draft as recommended by ACET. The workgroup will revise the "10/6/04 draft" based on ACET's comments and distribute "draft 2" to DGMQ for review and input. The workgroup will revise "draft 2" based on DGMQ's comments and circulate "draft 3" to ACET for a vote. Revision and distribution of all drafts and ACET's formal vote will be through electronic communications to ensure the recommendations are finalized and submitted to CDC prior to the February 2005 meeting. The final recommendations as approved by ACET will be distributed to the NCID, NCHSTP and OTPER Directors with a copy to the CDC Director.

Update on TBESC

Dr. Rachel Albalak of DTBE provided a status report on the research initiative. TBESC is a ten-year contract and was formally established in September 2001 as a result of CDC's response to the IOM report. CDC noted that "the nation lacks a clearly articulated research strategy" and acknowledged the need for "a coordinated research plan to maximize efficiency, ensure attention to highest priority activities and avoid duplication of effort." TBESC's mission is to conduct programmatically relevant epidemiologic, behavioral, economic, laboratory and operational research concerning the identification, diagnosis, prevention and control of TB disease and LTBI that lead to TB elimination. The TBESC sites include leading TB experts in the country and involve a collaboration between a state or metropolitan health department and academic institution. These partnerships build scientific research capacity and promote regional collaboration in TB research.

In response to DTBE's directive to reduce the TBESC budget by $1 million, the Arkansas and Minnesota Departments of Health and Universities of Alabama, British Columbia and Manitoba will be excluded from TBESC in FY'05. The selection was based on a formal evaluation of sites that would have the least impact on TBESC science and research as well as progress toward TB elimination. Despite the exclusion of the five sites, TBESC will remain strong. The consortium will continue to capture the majority of TB cases in the United States. Any of the five excluded TBESC sites that were awarded funds will only enroll patients if the cohort can be followed through the end of the study.

13 of 22 TBESC sites are also TBTC members. TBESC's organizational structure includes a steering committee of all 22 sites and CDC; the publications and presentations, bylaws, research, process evaluation, and external relations committees; and an executive committee of TBESC co-chairs and chairs of all five committees. Each TBESC site maintains a full-time project coordinator and part time principal investigator; an e-room accessed using a web-browser; a web-based data management system; a central IRB administered by CDC; and educational materials, protocols and standard operating procedures outlined in a monitoring and quality assurance contract. Eight sites are currently participating in the central IRB.

During TBESC's first semi-annual meeting in 2001, TB among foreign-born persons, LTBI and contact investigations were identified as the major research priorities. TBESC has since launched studies in all three of these areas. TBESC also established a diagnostics workgroup to guide the development of a work plan for diagnostic studies; address evolving diagnostic priorities; and establish collaborations with DTBE and external organizations. CDC and the Foundation for Innovative New Diagnostics (FIND) recently signed an MOU to advance the development of new diagnostic tools for LTBI, active TB and TB drug susceptibility testing. FIND is funding TBESC's study on a new and rapid solid culture system for TB.

Current activities vary among sites because the 16 TBESC studies are in different phases, including data collection, data analysis, development of interventions, IRB review, a pilot study, the approval process and protocol development. TBESC does not expect to develop new studies in the near future because data are now being collected from ongoing projects. The TBESC research agenda is currently being updated to respond to IOM, CDC and FTBTF recommendations, address gaps in knowledge, and meet program needs. TBESC's FY'05 budget projections are $6.8 million for research and $968,000 for infrastructure and support. The entire research budget is awarded to TBESC sites to conduct studies, while infrastructure and support dollars are used for the monitoring and quality assurance contract, travel and other internal expenses. However, the intramural budget does not cover salaries for DTBE staff.

In addition to the budget cut, TBESC faces other challenges. Complete intellectual freedom to establish a research agenda must be balanced with the need to respond to CDC priorities. Site-specific studies were launched to address TB research needs at both local and national levels. Development of long-term projects is an uncertain process because Congressional funding is appropriated on a yearly basis. Administration of TBESC is challenging because regulations and federal requirements must be met.

TBESC will undertake several efforts to strengthen its future direction. Study findings will be disseminated at various scientific conferences beginning in February 2005. Results will be applied to improve TB prevention and control. New collaborations will be established with CDC and external partners. Opportunities for outside funding will be solicited and research priorities will continue to be reviewed. An assessment will be conducted to determine whether adequate progress is being made toward the TBESC mission or if the mission should be revised to reflect evolving changes in TB control. Additional details on TBESC can be obtained from the NCHSTP web site at www.cdc.gov/nchstp.

ACET pointed out that local IRBs are established to address community concerns related to research. CDC should be aware that many communities will not relinquish control and accept a central IRB. CDC made several remarks in response to ACET's comments. The central IRB was established because data show that multiple IRBs can increase the time to read consent forms, result in more errors and delay the overall approval process. Moreover, local IRBs rarely have the necessary data to perform meaningful reviews of centrally managed multi-center trials. The majority of recent problems with clinical trials were at the local rather than central level.

The adoption of the central IRB by both TBESC and TBTC is a groundbreaking strategy within CDC, but the National Cancer Institute (NCI) has already implemented the model. NCI's central IRB was used as the basis in designing CDC's central IRB. One of CDC's IRBs developed the central IRB and is responsible for overseeing this activity for both TBESC and TBTC. Based on NCI's experience, CDC is aware that many local IRBs will view the central IRB as a mechanism to completely relinquish control to CDC and will not participate in the process. NCI nearly terminated its central IRB during the initial stage due to minimal participation and lack of confidence among local IRBs.

CDC designed its central IRB based on lessons learned by NCI. In both TBESC and TBTC, local IRBs maintain the right to review the original study protocol, make comments and address community concerns. Local IRBs can terminate enrollment in the central IRB at any time or only provide CDC with authority for consent forms, follow-up reviews or another specific component of the study. The central IRB will not minimize safeguards or other efforts to protect human subjects. CDC views the central

IRB as a promising and important tool in improving the overall research process and hopes advances will be made over time. For example, TBESC will benefit from and participate in NCHSTP's modest funding that was recently awarded to TBTC to conduct research on issues related to human subjects protection.

Update on TB Vaccine Activities

Dr. Michael Iademarco of DTBE described ongoing efforts to develop new TB vaccines. Bacille Calmette-Guerin (BCG) was first used orally as a vaccine in 1921 in Paris. WHO currently recommends that parenteral vaccination be administered once at birth because BCG prevents severe forms of pediatric TB. Data have shown that BCG also protects against leprosy. BCG is not administered in the United States, but is widely used in other parts of the world. BCG is manufactured by Aventis Pasteur and Organon Teknika and plays an extremely important role in the new TB vaccine effort. Many persons who would receive a new TB vaccine were intended to or have received BCG. A new TB vaccine could be linked to operational and organizational delivery structures previously established by BCG.

Over the past eight years, ACET and the Advisory Committee for Immunization Practices released two TB vaccine statements. The 1988 joint statement restricted use of BCG in the United States to children and advised against administering the vaccine to healthcare workers and HIV-infected persons. The 1996 joint statement noted that BCG is rarely used in the United States and recommended consultation with TB control programs if the vaccine is administered. The 1998 ACET-only statement acknowledged the importance of TB vaccines and recommended that public agencies and vaccine manufacturers develop a comprehensive and consensual strategy to achieve these goals. ACET's 1998 statement led to NIH developing the *U.S. Blueprint for TB Vaccine Development* in June 2000. CDC and FDA provided NIH with technical input during this effort.

The blueprint action plan called for vaccine-targeted laboratory research, production of vaccine candidates, animal studies, and Phase I, II and III clinical trials. Both the blueprint and ACET recommendations generated substantial commitment to implement the action plan, but several strategic issues must be considered in new vaccine development. Persons who are uninfected with *M.tb* can be primed and this action should be explored in a BCG replacement strategy. Persons infected with *M.tb* can be boosted with a new vaccine; estimates show that 2 billion individuals are currently infected. The prime and boost approaches can be combined. The background of BCG should be addressed. Live attenuated viruses and other special concerns should be acknowledged in HIV-infected populations. A determination should be made on

whether individuals with TB disease can be vaccinated to shorten the course or make the six-month chemotherapy more effective.

Vaccine formats currently being considered include recombinant modified BCG, a subunit of specific proteins in *M.tb* after BCG priming, attenuated *M.tb*, and DNA or other vector-based strategies. In the TB vaccine development effort, the need for new adjuvants to combine with a vaccine is becoming increasingly important to maximize efficacy. NIH has funded, supported and programmatically driven all U.S. activities related to new TB vaccine development. To date, centralized BCG has been characterized; a substantial amount of the basic science has been completed; several hundred candidates have been created; standardized testing has been performed in animals; and Phase I trials of three candidates have been initiated in uninfected and immunocompetent patients. A few candidates have shown promising results. Other complex issues related to BCG are also being addressed, particularly its immunologic correlative protection and immunologic response. Data have shown that BCG is not effective in adults, but is effective in young children for some period of time.

To support these efforts, WHO hosts the Stop TB Partnership and its new tools workgroup on TB vaccine research and development (R&D), drugs and diagnostics. The workgroup facilitates information exchange; provides a global platform to develop standards for preclinical testing and assessment of immunogenicity; coordinates support for NIH, Aeras Foundation and European TB Vaccine Cluster clinical trials; and tests and distributes BCG and Erdman *M.tb* working standards for preclinical studies under an FDA contract. The workgroup overlaps with the WHO advisory function and recently started to coordinate activities. FDA and NIH partner with the workgroup to address regulatory standardization to avoid future delays in the approval process.

The workgroup has several activities underway. The NIH blueprint is being used as a model to create a WHO road map for R&D of a global TB vaccine. The cost of developing a new TB vaccine has been estimated at $1 billion over 10 years, but consideration is being given to piloting an economic case study to demonstrate the actual cost from a global perspective. A trials site directory is being formulated to ensure the design and coordination of clinical trials are consistent. The Aeras Foundation was formerly the Sequella Foundation and employs former experts from several federal agencies and private pharmaceutical companies. Aeras was awarded an $83 million grant from the Gates Foundation to accelerate development of a new TB vaccine. This funding is currently being used to develop trial sites in the Republic of South Africa and launch a Phase I trial of one of the most promising TB vaccine candidates.

CDC's involvement in the TB vaccine development effort includes membership on the Stop TB workgroup; coordination with FDA and NIH on FTBTF; award of a $1 million

cooperative agreement to Aeras; identification of antigens through the DTBE Mycobacteriology Laboratory Branch; and dialogue with the CDC National Immunization Program (NIP) to discuss lessons learned from pertussis vaccine development that can be applied to TB. Based on Congressional language, CDC was required to award the cooperative agreement to an NGO that focused on R&D of a new TB vaccine. The funding will be used to prepare a site in India for a Phase III trial. NIP published CDC's 2002-2006 strategy for global immunization and described four elements of a new TB vaccine. In response to the document, consensus was established, a blueprint was developed and documented, research increased, and partnership building to increase capacity is ongoing.

Dr. Michael Kurilla, the ACET *ex officio* member for NIH, provided additional comments about the TB vaccine development effort. Several TB vaccine candidates have shown promise in animal studies, but the lack of animal models that can predict outcomes in human subjects with some degree of confidence is the most significant issue faced by the TB research community. NIH is continuing to fund research to refine animal models, particularly BCG vaccination protocols in naive humans in the United States. Candidates that are currently being administered to humans may not be solid enough for Phase III trials, but NIH hopes to use this experience to increase knowledge in conducting vaccine clinical trials in humans. Current efforts are also building a support structure that will meet regulatory requirements for full licensure when a stronger candidate is available in the future.

Update on Nucleic Acid Amplification Testing (NAAT)

CDC Perspective. Dr. Thomas Shinnick of DTBE provided a status report on ongoing efforts to revise guidelines for using NAAT to diagnose TB. FDA has approved the Gen-Probe Amplified *M.tb* Direct Test for use with AFB smear-positive and -negative specimens and the Roche *M.tb* Amplicor Test for use with smear-negative specimens only. Laboratory data show strong sensitivity of NAAT on a per patient basis in which ≥95% of AFB smear-positive TB cases are detected and 70%-90% of AFB smear-negative and culture-positive TB cases are detected.

Data from CDC's proficiency testing program show that commercially available tests are widely used by U.S. and international laboratories. Monthly averages for NAAT are 15 tests among 33 U.S. hospital laboratories, 103 tests among ten U.S. commercial laboratories, and 51 tests among 25 state public health laboratories. Actual numbers of tests performed by U.S. laboratories widely range from 1-871 tests per month, but the median of 7-28 tests per month is quite low. A July 2000 *MMWR* article outlined a reasonable approach based on available information. NAAT should be used for respiratory specimens from patients with signs or symptoms of active pulmonary TB, but

no presumed diagnosis. The *MMWR* article further recommended the following algorithm.

Sputum specimens should be collected on three different days for AFB spear and mycobacterial culture. NAAT should be performed on collection of the first sputum specimen, first smear-positive sputum specimen and additional sputum specimens as indicated. Clinicians should rely on clinical judgment in making decisions about the need for anti-TB therapy, further diagnostic work-up and isolation. The *MMWR* article did not recommend that NAAT replace AFB smear because AFB smear results are used in various settings, such as determining policies for isolation, release from isolation, infectiousness of a patient and contact investigations. NAAT only identifies the presence or absence of TB and is not designed as a quantitative tool.

The need for new NAAT guidance is now being considered because the current recommendations were published in 2000 and new data have been gathered since that time. Recent results show that NAAT can impact TB diagnosis and may be used for non-respiratory, pediatric and extrapulmonary specimens, including TB and meningitis. Several clinicians consider NAAT to be the standard of care in TB diagnostic work-up due to its ability to provide rapid confirmation of *M.tb* within 48 hours. Recently published research indicates that although a TB diagnosis is viewed as a clinically-based diagnosis, some clinicians delay treatment decisions until laboratory results are available. However, test results must be available as soon as possible to reduce delay in initiation of therapy. Unpublished laboratory data suggest that NAAT can confirm TB days or weeks before liquid or solid media.

Updated guidelines are also being considered because NAAT can impact treatment and control activities, facilitate prompt initiation of therapy, confirm a TB case for reporting purposes, and prioritize contact investigations. Programs have found commercially available NAAT kits to be particularly useful for rapid confirmation of smear-positive patients when the presence of TB or *M. avium* infection is uncertain. Some U.S. laboratories are using the molecular beacons model on an experimental basis or as a research tool to rapidly diagnose rifampin resistance. California and New York state laboratories have found this strategy to be successful in detecting mutations associated with rifampin resistance in a matter of hours without culture.

U.S. laboratories have also discovered that the molecular beacons model can be directly applied to sputum specimens. European laboratories have access to procedures, kits and other materials for rapid rifampin testing, but this technology is not available in the United States. Clinical trials to formally and widely evaluate NAAT's ability to rapidly determine drug resistance are not being considered at this time. NAAT recommendations are now being incorporated into new or revised guidelines for TB

diagnostic standards, TB control, infection control, contact investigations, surveillance and case detection, and *Healthy People 2010* (*HP2010*).

Efforts are underway at the federal level to support these activities. CDC convened a workshop in February 2004 with DTBE staff, clinicians, laboratorians, TB controllers and industry representatives to evaluate current data and existing guidelines. DTBE held internal discussions to review recommendations in available statements and guidelines, determine the science basis for revising current guidance, analyze new data, and identify data gaps in NAAT knowledge. To advance this effort, CDC will ensure consistency in current NAAT guidance; identify important unanswered questions; and establish the necessary science basis by evaluating existing data and promoting research. CDC will also engage ACET, APHL, ATS, IDSA, NTCA and other partners to review potential changes in the guidance and develop an implementation plan.

CDC acknowledges that several challenges must be addressed to successfully implement revised NAAT recommendations. Many laboratories will be reluctant to make changes, particularly since NAAT adds a significant cost. TB control programs and treatment centers rather than laboratories will benefit from any cost savings generated by NAAT. Overall costs and benefits of NAAT may vary by program. Optimal and cost-effective testing regimens have not been designed to date. Despite these challenges, CDC and its partners must collaborate in the development and implementation of revised NAAT guidance. This goal can be achieved if the value of NAAT to TB diagnosis, treatment and control is widely understood and opportunities are available to maximize the impact of rapid testing for TB controllers and clinicians.

NTCA Perspective. Ms. Kim Field, the NTCA President, described NAAT issues that will significantly impact TB controllers. The June 2000 *MMWR* article noted that the appropriate number of specimens to test with NAAT will vary based on the clinical situation, laboratory proficiency, and prevalence of TB and non-tuberculous mycobacterium. In June 2004, the Task Force on the Future of TB Laboratory Services recommended that all states and jurisdictions perform a true cost assessment of TB laboratory services. Each evaluation should include costs for laboratory services, training, communication systems, computers, surveillance databases, optimal testing, referral systems, implementation of new technologies, and public/private sector models.

HP2010 established a goal of obtaining laboratory confirmation of TB within 48 hours of receiving specimens for 75% of culture-confirmed cases. NAAT's ability to confirm TB within 48 hours will add to existing goals and objectives to report cases, meet *HP2010* goals and become the standard of care for TB among clinicians. Moreover, positive NAAT results are accepted as laboratory confirmation of TB cases for reporting purposes. For example, WSDH developed guidelines to use NAAT for all smear-positive specimens and smear-negative specimens only after individual consultation.

NTCA acknowledges that NAAT can facilitate and prioritize prompt initiation of therapy, isolation, case management and contact investigations. However, current guidance must be updated, particularly to advise clinicians who are unfamiliar with TB and will order or use NAAT with no regard to cost or added benefit.

As a follow-up to its June 2004 conference, NTCA wrote a letter to Dr. Castro to outline concerns about NAAT from the perspective of TB controllers. Key points and suggestions from the letter are highlighted as follows. A workgroup should be established to revise current recommendations. Guidelines published in the 2000 *MMWR* article do not provide sufficient or detailed advice to providers who may use NAAT. Updated guidelines will enable these providers to use NAAT to the greatest benefit without adding unnecessary cost. NAAT supplies should be centrally purchased and procured. For example, WSDH is charged an unreasonable cost of $85 per sample.

CDC should facilitate operational research on the cost-effectiveness of NAAT algorithms in selected patients and formally evaluate the impact of these approaches in TB diagnosis, isolation and contact investigations. CDC and its partners should facilitate the development of a guide for programs to interpret NAAT operational research results and take public health actions. CDC and its partners should disclose limitations of NAAT and describe circumstances where an alternative test would be required. Two NTCA members representing Massachusetts and Wisconsin have volunteered to collaborate with CDC and its partners in these efforts. NTCA's letter to Dr. Castro was distributed to ACET for review.

ACET agreed with NTCA's recommendation for CDC to update the 2000 NAAT guidelines because solid and detailed guidance has not been provided to date on using the test on a daily basis. TB controllers and programs will need strong recommendations from CDC before management will endorse and support additional costs associated with NAAT. Although sporadic use of NAAT indicates diagnostic testing is disparate across the country, implementation of NAAT over the past several years suggests that sufficient information is now available for the 2000 guidelines to be updated to reflect current data.

Solid guidelines from CDC will also make significant contributions at the federal level. For example, smear-negative and asymptomatic ICE detainees are usually deported before culture confirmation, but NAAT can more rapidly provide results prior to deportation. Rapid NAAT results can also play a role for ICE detainees or other persons completing TB therapy outside the United States because some countries will not continue treatment for unconfirmed cases.

ACET also agreed with NTCA's recommendation for CDC to conduct a NAAT cost-effectiveness study. Public health programs and laboratories are facing severe budget cuts and cannot add NAAT to existing activities. Most notably, $85 to test each specimen in which a majority will be smear-negative would be an astronomical cost to public health programs. Funding agencies will more readily reimburse NAAT and programs will be more willing to implement the test if CDC provides a solid science basis and gathers cost-effectiveness data.

ACET noted that NAAT has been extremely useful at the local level. Some programs have found NAAT to be most beneficial for TB suspects with weak signs or symptoms who do not warrant treatment in residential settings. In this scenario, NAAT results can strengthen the confidence of clinicians in not administering TB treatment to patients. CDHS and SFDPH found the molecular beacons model to be a solid tool for prioritizing MDR-TB in school and workplace settings. ACET was pleased that initial steps are being taken in this area since some laboratories are using the molecular beacons model as a research tool or on an experimental basis.

ACET made several recommendations for CDC to consider while updating the 2000 NAAT guidelines. Joint efforts by the TB and BT research communities on molecular testing for drug resistance should be reviewed and strategies should be explored to leverage funding for NAAT from this source. Laboratories should be reminded of the critical need to continue to obtain culture results despite the availability of NAAT. Secondary or backup guidelines to the NAAT recommendations should be formulated to advise public health programs and private clinicians on actions to take when NAAT cannot be fully implemented due to budget constraints or other issues. Aggressive actions should be taken to facilitate broader implementation of the molecular beacons model.

CDC made follow-up comments to ACET's deliberations. CDC agrees with ACET and NTCA that clear recommendations should be developed on interpreting and using NAAT. However, the reluctance of programs to order any type of TB diagnostic test is a critical issue that must also be addressed. As a result, revised NAAT guidelines should encourage practitioners to consider TB during the differential diagnosis of a patient who presents with clinical signs and symptoms and order appropriate tests.

CDC acknowledges that public health programs and laboratories are facing severe budget constraints, but NAAT's solid benefits should not be ignored because of cost. Expensive tests to detect myocardial infarction and other diseases are reimbursed, but these diseases also result in a tremendous number of negatives. The TB community should not settle for inexpensive methods to address this extremely important public health issue, particularly since strong efforts are being made to minimize delays in TB diagnosis in the United States. Instead, a proactive approach should be taken at the

national level to demonstrate the appropriate use and value of NAAT. HRSA-funded clinics, Medicaid and Medicare will be more likely to reimburse NAAT with this information.

CDC previously launched a cost-effectiveness study in which participants were and were not randomized to receive NAAT. The project was not successful because clinicians were unwilling to comply with guidelines, remove patients from isolation and take other actions in response to NAAT results. However, the study showed a significant impact on inappropriate initiation of therapy and length of isolation among HIV-infected persons. Results of the study were not published. DTBE recently drafted NAAT guidelines in follow-up to its February 2004 workshop and will establish a workgroup to revise the document. The two NTCA members who volunteered to assist DTBE in updating NAAT guidance will be asked to serve on the new workgroup.

ACET concluded the discussion with agreement to take the following actions. Ms. Freeman and Dr. Gonzales will represent ACET on DTBE's new NAAT workgroup. ACET's *ex officio* members for APHL and DIHS will also assign representatives to the workgroup.

Public Comment Period

The Chair opened the floor for public comments; no attendees responded.

New ACET Business

ACET proposed the following topics to add to the ongoing list of agenda items.

- Update by DTBE on awards to four TB regional training and medical consultation centers.
- Progress report on the DTBE/HAB collaborative project to improve TB services in HRSA-funded clinics.
- Presentation by Admiral Walling on the TATB strategic plan.
- Status report by Dr. Kawamura on follow-up communications with Admiral Walling.
- Update by DTBE on TBESC study findings.
- Presentation by FDA on regulatory issues related to new TB vaccine development.
- Presentation by the Alliance on new TB tools and diagnostics.

- Progress report by DTBE on NAAT workgroup activities. **[February 2005 meeting]**

Dr. Diana Schneider, the ACET *ex officio* member for DIHS, proposed two topics for ACET to consider. First, strategies should be explored to encourage U.S. Customs and Border Protection (CBP) to address TB. ACET previously communicated with Immigration and Naturalization Services, but Border Patrol issues are now under the jurisdiction of DHS. ICE has no authority over certain matters that are unique to CBP and is concerned about including CBP in existing workgroups. Regulatory and political issues associated with CBP may impede current activities. ACET could initiate dialogue with CBP with a letter outlining its concerns about TB and the lack of interaction between CBP and public health.

Second, a process should be developed to engage Department of Justice immigration judges in TB control efforts. The ideal approach would be for public health departments to advise judges on whether persons should be maintained in the United States to complete TB treatment. The recommendations would then be provided to ICE and immigration judges before the detainee's court hearing. This collaborative effort would be extremely beneficial to TB controllers. ICE legal counsel has asked to review any ACET communications prior to dissemination to immigration judges.

CDC was extremely concerned about ACET taking formal actions on the proposals at this time since both proposals involve complex interagency issues and are being made by federal agency officials to a FACA. Moreover, the CDC Office of General Counsel should be informed of any proposals or recommendations that ACET is considering that involve legal issues or the judicial system. CDC suggested the following modifications to the proposals to address these concerns.

For proposal 1, ACET should contact appropriate CBP officials before sending a letter to discuss TB and public health collaborations. ACET has never communicated with CBP and Border Patrol practices vary by state. ACET should obtain accurate information before communicating with CBP verbally or in writing and then structure the dialogue to be positive. For example, the remarkable progress in addressing TB among ICE detainees should be noted. Recent problems with Border Patrol should only be attributed to the federal reorganization. A formal invitation should be extended to include CBP in TB/PHP synergy and collaboration efforts. For proposal 2, HRSA, ICE and other agencies involved with immigration judges should engage in dialogue to clearly define federal roles before presenting this issue to ACET for formal action.

Based on CDC's comments, agreement was reached to take the following actions. ACET will extend written invitations to both CBP and ICE legal counsel to attend the next ACET meeting and broadly discuss the respective role of each agency in TB

control issues. For the first proposal, Drs. Escobedo and Schneider will gather accurate information after the CBP presentation, write a positive letter to CBP about its role in TB control and public health collaborations, and distribute the letter to ACET for approval prior to dissemination. For the second proposal, an update will be given at the next meeting on interagency discussions related to immigration judges. ACET will identify further actions to take at that time.

Closing Session

The next ACET meeting will be held either the week of February 7 or February 14, 2005; DTBE will poll the members by e-mail to confirm an exact date. With no further discussion or business brought before ACET, Dr. Kawamura adjourned the meeting at 11:45 a.m. on October 7, 2004.

I hereby certify that to the best of my knowledge, the foregoing Minutes of the proceedings are accurate and complete.

_____
Date

_____
L. Masae Kawamura, M.D.
ACET Chair

ATTACHMENT 1

ACET's 10/6/04 Draft Recommendations

ACET requests that CDC:

1. Define "full" use of emergency preparedness funding, and criteria used for audit disallowances. Disseminate results to all CDC-funded public health programs.
2. Structure collaboration into required recipient activities for all cooperative agreements.
3. Identify at the federal and state level, areas for potential synergy between emergency preparedness and other public health programs, and disseminate them for federal state and local action. Examples include public health law, training, border health, and quarantine station expansion (see below).
4. Quantitatively evaluate and report on the impact of public health preparedness programs on the rest of the public health system (including on TB control programs).
5. Inform all CDC-funded public health programs of the emergency preparedness performance measures, and work to link these to CDC performance measures in the rest of the CDC-funded programs.
6. Explore the possibility of expanding a cadre of "pluripotential" staff such as public health advisors, trained to respond to future terrorist event as well as in the day to day control of present day threats (TB, STDs, etc). (See joint STD and TB controllers associations discussion paper: "Hiring of Communicable Disease Investigators: One potential use for a portion of bioterrorism funds." www.ntca-tb.org).

In addition, we request that CDC make "full use" of the quarantine station expansion. Specifically, we advise that CDC convene an interagency work group of the appropriate partners (Dept of Homeland Security, US Customs and Enforcement, Border Patrol) to coordinate multidisciplinary teams working with or at quarantine stations. Coordinated activities include disease identification, response to health emergencies, monitoring/ enforcing requirements of travelers, and communicating disease intelligence information to partners including local and state health departments.

With the expansion currently underway, we also request that CDC consider the following proposals that are consistent with DGMQ intent, that would also benefit TB control:

1. Funding for the development and implementation (training, data entry) of the Electronic Data Network. First in line for development is the TB component, on

which we understand additional components will be built, such as an information system for arriving passengers ill with other communicable diseases.

2. Expanded quarantine station staff (medical epidemiologists and public health advisors) who could enhance the B notification system by:
   - Conducting follow up investigations to determine systems failure when immigrants and refugees (despite overseas screening) have infectious TB upon arrival. These “table top exercises” provide opportunities to identify and close gaps in the public health defenses that allowed importation of disease from other parts of the world.
   - Working with state and local TB programs to assess and improve the domestic follow up of B notification patients, in order to maximize the TB cases detected and future cases prevented.
   - Providing a “look-out” system to identify, upon re-entry or departure, TB patients who have been lost to follow up before completing evaluation or treatment for TB.
3. Expanded quarantine station staff who could also:
   - Identify arriving passengers who are ill with respiratory illnesses (including TB).
   - Coordinate TB contact investigations among airline passengers and evaluating results.